## REMARKS

**Pending Claims**

Added Claims 44-59 depend directly or indirectly from Claim 8.

**Restriction Requirement**

In the Restriction Requirement, the Examiner requested Applicants to elect one of the following inventions:

Group I (claims 1-3, 14, and 15) drawn to an isolated polypeptide comprising an amino acid sequence of SEQ ID NO:1 and SEQ ID NO:3);

Group II (claims 4, 5, 7, 9, and 10) drawn to an isolated polynucleotide, host cell, and method for producing a polypeptide;

Group III (claim 8 ) drawn to an antibody;

Group IV (claims 11 and 12 ) drawn to a method for detecting a target polynucleotide in a sample comprising hybridizing the sample with a probe comprising at least 20 contiguous nucleotides;

Group V (claim 13 ) drawn to a method for detecting a target polynucleotide in a sample comprising amplifying said target polynucleotide using polymerase chain reaction amplification;

Group VI (claim 17) drawn to a method for screening a compound for effectiveness as an agonist of a compound;

Group VII (claim 20 ) drawn to a method for screening a compound for effectiveness as an antagonist of a compound;

Group VIII (claim 23 ) drawn to a method for screening for a compound that specifically binds to a polypeptide;

Group IX (claim 24 ) drawn to a method for screening for a compound that modulates the activity of a polypeptide;

Group X (claim 25 ) drawn to a method for screening a compound for effectiveness in altering expression of a target polynucleotide; and

Group XI (claim 26 ) drawn to a method for assessing toxicity of a test compound.

**Applicants hereby elect, with traverse, to prosecute Group III, which includes and is drawn to Claim 8. In addition, in response to the "restriction requirement" to elect a particular SEQ ID NO:, Applicants provisionally elect the portion of the claims directed to SEQ ID NO:1, also with traverse.**

Applicants traverse the requirements on the following grounds:

Applicants submit that the invention encompassed by added Claims 44-59, drawn to antibodies and methods of use, could be examined at the same time as the invention encompassed by the claim of Group III without undue burden on the Examiner.

Accordingly, because the search required to identify prior art relevant to the claims of Group III (Claim 8), as well as newly added Claims 44-59, would substantially overlap, Applicants respectfully submit that examination of Claims 8 and 44-59 would pose no undue burden. Thus, Applicants request reconsideration of the Restriction Requirement and examination of Claims 8 and 44-59.

However, in addition, Applicants also traverse this restriction requirement insofar as it is, in effect, a requirement for election of species as between elements in Markush groups (those elements being, respectively, SEQ ID NO:1 and SEQ ID NO:3 with respect to the polypeptides). The Examiner's attention is directed to the Patent Office's own requirements for Markush practice, set forth in the 8th edition of the M.P.E.P. (August 2001) at § 803.02 regarding restriction requirements in Markush-type claims:

> PRACTICE RE MARKUSH-TYPE CLAIMS
>
> If the members of the Markush group are **sufficiently few in number or so closely related** that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claim on the merits, even though they are directed to independent and distinct inventions. In such a case, the examiner will not follow the procedure described below and will not require restriction.
>
> Since the decisions in *In re Weber*, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and *In re Haas*, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), **it is improper for the Office to refuse to examine that which applicants regard as their invention**, unless the subject matter in a claim lacks unity of invention. *In re Harnish*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, **unity of invention exists where**

**compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility.**

This subsection deals with Markush-type generic claims which include a plurality of alternatively usable substances or members. In most cases, a recitation by enumeration is used because there is no appropriate or true generic language. A Markush-type claim can include independent and distinct inventions. This is true where two or more of the members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the claim obvious under 35 U.S.C. 103 with respect to the other member(s). In applications containing claims of that nature, **the examiner may require a provisional election of a single species** prior to examination on the merits. The provisional election will be given effect in the event that the Markush-type claim should be found not allowable. Following election, the Markush-type claim will be examined fully with respect to the elected species and further to the extent necessary to determine patentability. If the Markush-type claim is not allowable over the prior art, examination will be limited to the Markush-type claim and claims to the elected species, with claims drawn to species patentably distinct from the elected species held withdrawn from further consideration.

As an example, in the case of an application with a Markush-type claim drawn to the compound C-R, wherein R is a radical selected from the group consisting of A, B, C, D, and E, the examiner may require a provisional election of a single species, CA, CB, CC, CD, or CE. The Markush-type claim would then be examined fully with respect to the elected species and any species considered to be clearly unpatentable over the elected species. If on examination the elected species is found to be anticipated or rendered obvious by prior art, the Markush-type claim and claims to the elected species shall be rejected, and claims to the nonelected species would be held withdrawn from further consideration. As in the prevailing practice, a second action on the rejected claims would be made final.

On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a *non-elected species,* the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. The prior art search, however, will not be extended unnecessarily to cover all nonelected species. Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim, the

> claim will be rejected and the action made final. Amendments submitted after the final rejection further restricting the scope of the claim may be denied entry. [emphasis added]

As can be seen from the above, it is clear that the present Restriction Requirement does not meet the Patent Office's own requirements.

The Examiner noted that "[t]he claims are generic to a plurality of disclosed patentably distinct species." (Office Action, page 3.)

However, it is first noted that if the number of "members of the Markush group are **sufficiently few in number or so closely related** that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claim on the merits, even though they are directed to **independent and distinct inventions. In such a case, the examiner will not follow the procedure described below and will not require restriction.**" Withdrawal of the restriction requirement is required on that basis alone.

Second, **it is improper for the Office to refuse to examine that which applicants regard as their invention**, unless the subject matter in a claim lacks unity of invention. The antibodies of the present invention share a common utility, for example, as research tools in the discovery of compounds that bind to and/or modify the activity of SH3 domain-containing proteins and in toxicology studies based on expression profiling.

Third, even if the claims could be considered to be "Markush-type generic claims which include a plurality of alternatively usable substances or members," it is further noted that the M.P.E.P states that "A Markush-type claim can include independent and distinct inventions. This is true where two or more of the members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the claim obvious under 35 U.S.C. 103 with respect to the other member(s). In applications containing claims of that nature, **the examiner may require a provisional election of a single species** prior to examination on the merits." This clearly applies in the present case.

Finally, Examiner's attention is directed to the M.P.E.P. at § 803.04 (Restriction - Nucleotide Sequences, EXAMPLES OF NUCLEOTIDE SEQUENCE CLAIMS) which states:

> Applications claiming more than ten individual independent and distinct nucleotide sequences in alternative form, such as set forth in example (A), will be subject to a restriction requirement. Only the ten nucleotide sequences selected in response to the restriction requirement and any other claimed sequences which are patentably indistinct therefrom will be examined.
>
> Applications claiming only a combination of nucleotide sequences, such as set forth in example (B), will generally not be subject to a restriction requirement. The presence of one novel and nonobvious sequence within the combination will render the entire combination allowable. The combination will be searched until one nucleotide sequence is found to be allowable. The order of searching will be chosen by the examiner to maximize the identification of an allowable sequence. If no individual nucleotide sequence is found to be allowable, the examiner will consider whether the combination of sequences taken as a whole renders the claim allowable.

The instant application claims antibodies directed to two polypeptide sequences and the claims examined clearly should not be limited by an election of antibodies directed to only a single sequence under the guidelines set forth in the M.P.E.P. at § 803.04.

Therefore, it is respectfully submitted that, upon searching and examining antibodies directed to SEQ ID NO:1 and finding no prior art over which antibodies directed to SEQ ID NO:1 can be rejected, the Examiner must extend the search of the Markush-type claim to include the non-elected species, antibodies directed to SEQ ID NO:3.

Applicants reserve the right to prosecute the subject matter of non-elected claims in subsequent divisional applications.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108.**

Respectfully submitted,

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## VERSION WITH MARKINGS TO SHOW CHANGES MADE

## IN THE CLAIMS:

**Claims 44-59 have been added.**

44. (New) A diagnostic test for a condition or disease associated with the expression of HS3C in a biological sample comprising the steps of:

a) combining the biological sample with an antibody of claim 8, under conditions suitable for the antibody to bind the polypeptide and form an antibody:polypeptide complex; and

b) detecting the complex, wherein the presence of the complex correlates with the presence of the polypeptide in the biological sample.

45. (New) The antibody of claim 8, wherein the antibody is:

a) a chimeric antibody,

b) a single chain antibody,

c) a Fab fragment,

d) a $F(ab')_2$ fragment, or

e) a humanized antibody.

46. (New) A composition comprising an antibody of claim 8 and an acceptable excipient.

47. (New) A method of diagnosing a condition or disease associated with the expression of

HS3C in a subject, comprising administering to said subject an effective amount of the composition of claim 46.

48. (New) A composition of claim 46, wherein the antibody is labeled.

49. (New) A method of diagnosing a condition or disease associated with the expression of HS3C in a subject, comprising administering to said subject an effective amount of the composition of claim 48.

50. (New) A method of preparing a polyclonal antibody with the specificity of the antibody of claim 8, the method comprising:

a) immunizing an animal with a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:3, or an immunogenic fragment thereof, under conditions to elicit an antibody response,

b) isolating antibodies from said animal, and

c) screening the isolated antibodies with the polypeptide, thereby identifying a polyclonal antibody which binds specifically to a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:3.

51. (New) An antibody produced by a method of claim 50.

52. (New) A composition comprising the antibody of claim 51 and a suitable carrier.

53. (New) A method of making a monoclonal antibody with the specificity of the antibody of claim 8, the method comprising:

a) immunizing an animal with a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:3, or an immunogenic fragment thereof, under conditions to elicit an antibody response,

b) isolating antibody producing cells from the animal,

c) fusing the antibody producing cells with immortalized cells to form monoclonal antibody-producing hybridoma cells,

d) culturing the hybridoma cells, and

e) isolating from the culture monoclonal antibody which binds specifically to a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:3.

54. (New) A monoclonal antibody produced by a method of claim 53.

55. (New) A composition comprising the antibody of claim 54 and a suitable carrier.

56. (New) The antibody of claim 8, wherein the antibody is produced by screening a Fab expression library.

57. (New) The antibody of claim 8, wherein the antibody is produced by screening a recombinant immunoglobulin library.

58. (New) A method of detecting a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:3 in a sample, the method comprising:

a) incubating the antibody of claim 8 with a sample under conditions to allow specific binding of the antibody and the polypeptide, and

b) detecting specific binding, wherein specific binding indicates the presence of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:3 in the sample.

59. (New) A method of purifying a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:3 from a sample, the method comprising:

a) incubating the antibody of claim 8 with a sample under conditions to allow specific binding of the antibody and the polypeptide, and

b) separating the antibody from the sample and obtaining the purified polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:3.